14

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
TSJ/TP/37355		

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/01086	22/03/2000	22/03/1999

International Patent Classification (IPC) or national classification and IPC
A61K31/695

Applicant
CHARTERHOUSE THERAPEUTICS LTD. et al.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 7 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
17/10/2000	23.07.2001

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/01086

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-39	as originally filed				

Claims, No.:

1-36	as received on	19/06/2001	with letter of	19/06/2001	

Drawings, sheets:

1/11-11/11	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-30 and 32-35 (all in parts), 31, 36.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 31, 36 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-30 and 32-35 (all in parts).

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1-9, 12-30, 32-35

	No:	Claims	10, 11
Inventive step (IS)	Yes:	Claims	1-9, 13
	No:	Claims	10-12, 14-30, 32-35
Industrial applicability (IA)	Yes:	Claims	1-30, 32-35
	No:	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. No opinion can be established on claim 36, which is obscure due to a lack of technical features.
2. No opinion can be established on claim 31, which is obscure due to the reference to the figures as well as to the negative characteristic.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The opinion expressed as to novelty, inventive step and industrial applicability refers only to matter for which an international search report has been drawn up (Rule 66.1(e) PCT).

2. Reference is made to the following documents:
   D1: EP-A-0 180 399
   D3: WO 99 00349 A & Database WPI, Derwent Publications LTD, London, GB, abstract AN:1999-095632 [08]
   D4: WO 98 40346 A & Database WPI, Derwent Publications LTD, London, GB, abstract AN: 1998-506654 [43]
   D5: US-A-5 216 183
   D8: WO 99 04777 A & Database WPI, Derwent Publications LTD, London, GB, abstract AN: 1999-142580 [12]

3. Novelty
   D5 (Example 1 of Table I, no specific enantiomer specified) discloses the compounds claimed in claim 10 and 11. Novelty can therefore not be acknowledged for claims 10 and 11.
   The subject-matter of claims 1-9 and 12-30 and 32-35 is not disclosed by any of the documents cited in the search report, and is therefore considered to be novel.

4. Inventive step

4.1. The document **D1** is regarded as being the closest prior art to the subject-matter of claim 1, and discloses 4-Hydroxy-2-cyclopentenones used for the treatment of malignant tumours, where compound (I) has the following substituents: X (corresponding to R_6 of formula b in claim 1) is hydrogen or halogen, A (corresponding to R_1) is hydrogen, B and R^1 (corresponding to R_2) represent a hydroxyl group and a substituted, unsubstituted alkyl, alkenyl or alkynyl group, respectively, R^2 (corresponding to R_3) is again a substituted, unsubstituted alkyl, alkenyl or alkynyl group, and R^3 (corresponding to X) can be a protective group such as disclosed in **D1** on p. 10, lines 8-20). (abstract; Claims 1-10; p. 6, line 21 - p. 7, line 5; p. 10, lines 16-20; p. 23, lines 22-26; see also compounds (202), (208), (214) and (220)

The compounds of **D1** differ from the compounds a, b, c or d disclosed in claim 1 in the following way: at position R_3, the compounds of **D1** contain a hydrocarbon group with C_1-C_{10} instead of hydrogen, and at positions R_1 and R_2, the compounds of **D1** contain a hydrogen atom and an alkoxy group. The expert in the field would therefore need to modify the compounds of **D1** in two ways to get to the claimed compounds. Since there is no hint in the documents cited in the search report on how to arrive at the claimed compounds, the subject-matter of claim 1 and dependent claims 2-9 are therefore considered to be inventive.

4.2. Claim 13 is also considered to be inventive, since the necessary modification to arrive at the claimed structures are not disclosed in the prior art.

4.3. Claim 12 is not considered to be inventive in the light of documents **D5** in combination with **D3, D4** or **D8**. **D5** discloses the compound per se, and although the compound of example 1 is used in **D5** as a prodrug, (the active compounds of **D5** being substituted at the double bond), the expert in the field would, based on the closely related compounds disclosed in **D3**, **D4** and **D8** (which all are not substituted at said double bond, but nonetheless show the therapeutic activity common to the class of cyclopentenone derivatives), expect that the compound of example I disclosed in **D5** would also exhibit such an activity. Furthermore, the use of an S-enantiomer in medicine would be obvious for the skilled person, unless the applicant shows any unexpected effect or advantage over the prior art pharmaceutical compositions. No inventive activity can therefore be acknowledged for claim 12.

4.4. In the light of **D3**, which discloses the use of cyclopentenone derivatives for the treatment of cancer, viral diseases, rheumatic disorders, autoimmune disorders, diabetes, allergies and inflammation, and where it is stated that the compounds activate heat shock protein (abstract), and of **D4**, which discloses that cyclopentenone-derivatives are used in the treatment of bacterial infections (abstract), claims 14-24 and 26-29 and 32 are not considered to be inventive, due to their reference to claim 12. Furthermore, inventive step cannot be acknowledged for claim 25, since the application does not contain any evidence that the claimed effect does take place.

4.5. Since the effect of heat shock protein activation is known from **D3**, the subject-matter of claim 30 is not considered to be inventive in the light of **D3** combined with **D5**, for the reasons set forth under 4.2 and 4.4.

4.6. Although the prior art is silent about the use of the claimed compounds as food for aquatic organisms, inventive step cannot be acknowledged for claims 33-35 because the application does not show that such a nutritional effect actually takes place, nor is it obvious that these compound, in addition to their pharmacological effects, would also have nutritional value (separate from therapeutic value as antivirals or food and or water conservative, such as disclosed in **D4**), nor is it clear what an aquaculture system refers to.

5. Industrial applicability

For the assessment of the present claims 14-30 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VI

Certain documents cited

Certain published documents (Rule 70.10)

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO 99/29647	17.06.1999	12.08.1998	11.12.1997
EP-A-1008 345	14.06.2000	18.03.1998	02.07.1997
EP-A-0978 278	09.02.2000	18.03.1998	28.03.1997
EP-A-0978 277	09.02.2000	18.03.1998	01.04.1997

Re Item VIII

Certain observations on the international application

1. Claim 31 contains references to the drawings. According to rule 6.2(a) PCT, claims should not contain such references except where absolutely necessary, which is not the case here.

2. Claim 36 is not clear due to the lack of technical features .

3. Claim 3 and dependent claims 4-9, 12, 14-30, and 32-35 do not meet the requirements of Art. 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved: "wherein the ocmpound has higher activity than cyclopent-2-en-1-one in respect to one or more of the following...", which merely amounts to a statement of the underlying problem. The technical features necessary for achieving this result should be added.

4. The following claimed therapeutic uses are not specified therapeutic applications, thereby rendering said claims unclear:
   Claim 3: activating HSF, inhibiting NF-kB, inhibiting the replication of HSV-1, inhibiting the replication of Sendai virus.

Claim 26: a disorder affecting aquatic organisms
Claim 28: plant disorder

5. The term "aquaculture system" (claim 35) is not clear.